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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Richard M. Lawn, Gordon A. Vehar, and Karen L. Wion

Serial No: 08/444,934 Art Unit: 1653

Filed: May 22, 1995 Examiner: H. Schnizer

For: *METHODS AND DEOXYRIBONUCLEIC ACID FOR THE PREPARATION OF TISSUE FACTOR PROTEIN*

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY TO EXAMINER'S ANSWER

Sir:

This is in reply to the Examiner's Answer mailed December 29, 1999.

There is agreement that the only issue on appeal is whether or not claims to a truncated human tissue factor are described under 35 U.S.C. §112, by the specification as filed. The language of the specification refers at multiple points to human tissue factor variants, and deletions of portions of the 263 amino acid protein, but does not explicitly state that one should delete the transmembrane and cytoplasmic domains to yield a soluble human tissue factor. There is no dispute that the specification discloses making a soluble human tissue factor having the transmembrane or hydrophobic domain deleted. There is also no dispute that one skilled in the art would be led to make a soluble human tissue factor having the transmembrane and cytoplasmic domains deleted.

In fact, the Examiner expressly agreed that one of skill in the art would understand "that such a diagram (referring to Figure 5) would make it obvious to make a tissue factor variant containing only the extracellular domain." (Page 15 of the Examiner's Answer).

The test of whether or not a specification discloses the claimed subject matter is whether one skilled in the art would read the specification as disclosing the claimed subject matter. Appellants have provided objective third party evidence that those skilled in the art would read the specification in issue and make the claimed human tissue factor consisting solely of the extracellular domain.

(1) Dr. Konigsberg's Declaration, a copy of which is attached.

Dr. Konigsberg stated at page 2, paragraph 5, "I believe that those of skill in the arts of proteins, cloning and expression, and tissue factor at that time (when the parent application was filed) would have understood the descriptions of deletion of the transmembrane region of tissue factor to include tissue factor proteins from which the entire C-terminal region, including the transmembrane and cytoplasmic regions, had been deleted. This is so because the deletion of the transmembrane region as described in the specification would have been viewed and understood as an indication that the extracellular domain could be used separately from both the transmembrane region and the cytoplasmic region." "From this scheme, it is clear, and those of skill in the art at the time would have understood, that deletion of the transmembrane region is equivalent to deletion of both the transmembrane region and the cytoplasmic region, since the cytoplasmic domain serves no purpose in the absence of the transmembrane domain." (page 4)

(2) The opposition filed in the corresponding European patent application.

The claims to the human tissue factor, including the truncated tissue factor, were granted in the corresponding European patent application which was then opposed by Diagnostica Stago. The opposition argues that the claim to the truncated protein is obvious (assuming that cloning of the gene encoding the entire human tissue factor is obvious, which is not in dispute in this application) in view of prior art (DS9) that it was known to delete both the hydrophobic and cytoplasmic domain of a protein while preserving the biological activity of the complete mature protein (section 3.1), and that "Once the person skilled in the art has determined the sequence of hTF he has no difficulty in obtaining variants or fragments of this protein. These variants or fragments can be obtained (i) if necessary by enzymatic slicing, particularly to separate the transmembrane and cytoplasmic domains in accordance with DS9 and (ii) in particularly by genetic engineering (recombinant process) after having constructed and inserted the portions of DNA into an expression vector, encoding each one for the variant or fragment in question." (section 3.6).

The examiner has provided nothing to rebut these opinions that it was obvious to one skilled in the art to make the truncated tissue factor based on the specification as filed, and that this would have been routine once one had succeeded in cloning the tissue factor.

Allowance of all claims is earnestly solicited.

Respectfully submitted,

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I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

Patrea L. Pabst

Date: February 29, 2000